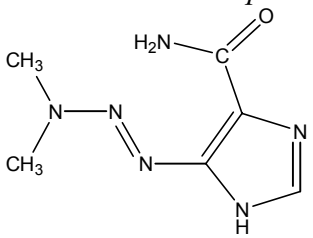
DACARBAZINE
CAS No. 4342-03-4
First Listed in the *Fourth Annual Report on Carcinogens*



CARCINOGENICITY

Dacarbazine is *reasonably anticipated to be a known human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals (IARC V.26, 1981; IARC S.4, 1982; IARC S.7, 1987). When administered orally in the diet, dacarbazine induced thymic and splenic lymphosarcomas and mammary adenocarcinomas in rats of both sexes and cerebral ependymomas and pulmonary alveolar carcinomas in female rats. When administered by intraperitoneal injection, dacarbazine induced lung tumors, lymphomas, and splenic hemangiomas in male mice and lung tumors and uterine tumors in female mice. In a separate study, intraperitoneal injection of dacarbazine induced mammary adenocarcinomas and adenofibromas, thymic and splenic lymphosarcomas, leiomyosarcomas of the uterus, cerebral ependymomas, ependymoblastomas, embryonal adenosarcomas, adrenal cortical adenomas, bronchogenic adenocarcinomas, and renal cortical adenocarcinomas in female rats. Intraperitoneal injection of dacarbazine in another study involving rats induced lymphomas and heart tumors in both sexes, renal tumors in males, and breast carcinomas in females (IARC V.26, 1981).

There is inadequate evidence for the carcinogenicity of dacarbazine in humans (IARC S.4, 1982; IARC S.7, 1987). A single case of acute leukemia after treatment with dacarbazine in combination with other cytotoxic agents has been reported (IARC V.26, 1981).

PROPERTIES

Dacarbazine occurs as white to ivory-colored microcrystals that are soluble in water. Dacarbazine is extremely light sensitive and rapidly undergoes photodecomposition. Dacarbazine is sensitive to oxidation but is stable in neutral solutions in the absence of light. When heated to decomposition, it emits toxic fumes of nitrogen oxides (NO_x).

USE

Dacarbazine is used as an antineoplastic agent in the treatment of diseases such as malignant melanomas, Hodgkin's disease, soft-tissue sarcomas, osteogenic sarcomas, and neuroblastomas. It is occasionally used in the therapy of other neoplastic diseases that have become resistant to alternative treatment (IARC V.26, 1981).

PRODUCTION

Dacarbazine is not currently produced domestically, but it is imported (IARC V.26, 1981). Import volumes, however, have not been reported. The 1998 *Chemical Buyers Directory* names one U.S. supplier of the compound (Tilton, 1997).

EXPOSURE

The primary routes of potential human exposure to dacarbazine are injection, inhalation, and dermal contact. For patients receiving dacarbazine, the usual initial dose is 2-4.5 mg/kg body weight intravenously or intra-arterially daily for 10 days and repeated after intervals of 4 weeks, or 100-250 mg/m^2 of body surface for 5 days and repeated after intervals of 3 weeks (IARC V.26, 1981). Potential exposure of health professionals who handle this drug (e.g., pharmacists, nurses, and physicians) may occur during drug preparation, administration, or cleanup; however, the risks can be avoided through use of appropriate containment equipment and work practices (Zimmerman et al., 1981). Potential occupational exposure may also occur for workers involved in the formulation or packaging of the pharmaceuticals.

REGULATIONS

This chemical is used as a pharmaceutical, and in low quantities relative to other chemicals; therefore, it is of little regulatory concern to EPA. However, there may be a small pollution problem relative to hospital wastes. FDA regulates dacarbazine under the Food, Drug, and Cosmetic Act (FD&CA) as a drug approved for human use. FDA requires warning labels on dacarbazine regarding its potential carcinogenicity, mutagenicity, teratogenicity, and/or impairment of fertility. OSHA regulates dacarbazine under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table B-32.